Remarks

Amendments to the Claims

Independent claims 27, 56, 62, and 63 are amended to recite that the antisense oligonucleotides "are complementary to a coding sequence for human MDM2." Claims 27 and 56 also are amended to recite that the antisense oligonucleotides inhibit "expression of MDM2 protein."

The specification supports these amendments by its disclosure of the coding sequence for human MDM2 and on page 10, lines 25-28: "For example, expression may be down-regulated by administering triple-strand forming or antisense oligonucleotides which bind to the hMDM2 gene or mRNA, respectively, and prevent transcription or translation. The oligonucleotides may interact with unprocessed pre-mRNA or processed mRNA."

The amendments do not add new matter.

Priority

As requested, the specification is amended to update the application's priority information.

The Rejection of Claims 27, 28 56, 62, and 63 Under 35 U.S.C. § 112 ¶ 1

Claims 27, 28, 56, 62, and 63 are rejected under 35 U.S.C. § 112 ¶ 1 as neither described nor enabled.[1] Applicants respectfully traverse the rejections.

The Office Action contends that the claims as previously presented read on using antisense oligonucleotides which bind to portions of the human MDM2 gene which the specification does not disclose. To advance prosecution, independent claims 27, 56, 62, and 63 are amended to recite that the antisense oligonucleotides "are complementary to a coding sequence for human MDM2." As the Office Action acknowledges, the skilled artisan can envision any oligonucleotide that is complementary to the human MDM2 coding sequence. Office Action at page 4, lines 13-14 and page 7, lines 17-18. The Office Action contends, however, that "the skilled artisan would be unable to determine without further experimentation if the sequence had a function that was considered essential for the claimed genus of oligonucleotides." Office Action at page 4, lines 14-16. The claimed function encompasses inhibition of (claims 27 and 56) or interference with (claims 62 and 63) MDM2 protein expression (*e.g.*, via inhibition of or interference with transcription or translation).

The response filed April 5, 2006 provided post-filing date references which demonstrate that *MDM2* antisense oligonucleotides are not difficult to identify and do, in fact, inhibit MDM2 expression.[2] The Office Action dismisses this evidence because (1) the post-filing date references employ antisense oligonucleotides against the coding sequences of

[1] The Office Action does not explicitly reject the claims as not enabled, but the text of the rejection makes that assertion.

[2] **Capoulade** *et al.*, *Blood 97* (2001):1043-10495; **Chen** *et al.*, *Proc. Natl. Acad. Sci. USA 95* (1998):195-200; **Sato** *et al.*, *Anticancer Research 20*, 837-42, 2000; **Goetz** *et al.*, *Cancer Res. 61*, 7635-41, October 15, 2001; **Wang** *et al.*, *Int. J. Oncol. 15* (1999):653-660; **Zang** *et al.*, *Proc. Natl. Acad. Sci. USA 100*, 11636-41, September 30, 2003; **Miraglia** *et al.*, U.S. Patent No. 6,238,921; **Fiddler** *et al.*, *Mol. Cell. Biol. 16*, 5048-57, September 1996; **Zang & Wang**, "in Methods in Molecular Medicine 85: Novel Anticancer Drug Protocols, pages 205-22, Buolamwini & Adjei, eds., Humana Press, 2003.

hMDM2 and (2) the specification does not teach the skilled artisan to make and distinguish between antisense oligonucleotides which are active and those which are not. Office Action at page 8 ¶¶ 1 and 2.

With respect to the first point, the claims as amended recite "a coding sequence for human MDM2." Thus, the claims as amended are commensurate in scope with post-filing date references which teach use of antisense oligonucleotides against the coding sequences of hMDM2.

With respect to the second point, the specification teaches assays by which MDM2 expression can be detected; see Examples 5 and 9. The specification provides antibodies which can be used to detect MDM2 protein; see Example 8. At the April 7, 1992 priority date of this application, those skilled in the art were well-versed at testing antisense oligonucleotides for their effect on protein expression. See the references provided as Exhibits A through L with the response filed May 31, 2005. The skilled worker would therefore easily have been able to use the assays and antibodies disclosed in the specification to test whether any particular oligonucleotide inhibited expression of MDM2 protein (claims 27, 28, and 56) or interfered with expression of MDM2 (claims 62 and 63).

The specification both describes and enables the claims as amended to one skilled in the art. Applicants respectfully request withdrawal of the rejections.

Respectfully submitted,
BANNER & WITCOFF, LTD.
/Lisa M. Hemmendinger/

Dated: November 13, 2006 By: _____
Lisa M. Hemmendinger
Registration No. 42,653

Customer No. 22907